Emtricitabine (FTC, Emtriva)

For additional information see Drugs@FDA:
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Formulations

Pediatric oral solution: 10 mg/mL

Capsules: 200 mg

Combination tablets:
- *With tenofovir (TDF):* FTC 200 mg + TDF 300 mg (Truvada)
- *With TDF and efavirenz (EFV):* FTC 200 mg + TDF 300 mg + EFV 600 mg (Atripla)

Dosing Recommendations

Neonate/infant dose (0–3 months of age):
Oral solution: 3 mg/kg once daily.

Pediatric dose (≥3 months–17 years of age):
Oral solution:
6 mg/kg (maximum dose 240 mg) once daily.

Capsules (for children who weigh >33 kg):
200 mg once daily.

Adolescent (≥18 years of age)/adult dose:
Oral solution: 240 mg (24 mL) once daily.
Capsules: 200 mg once daily.

Combination Tablets
Truvada (FTC + TDF)
Adult dose: 1 tablet once daily.

Atripla (FTC + TDF + EFV)
Adult dose: 1 tablet once daily.

See efavirenz section for pregnancy warning.

Selected Adverse Events

- Minimal toxicity.
- Severe acute exacerbation of hepatitis can occur in hepatitis B virus (HBV)-coinfected patients who discontinue FTC.
- Hyperpigmentation/skin discoloration on palms and/or soles, predominantly observed in nonwhite patients.

Special Instructions

- FTC can be given without regard to food; however, administer Atripla on an empty stomach because it also contains EFV.
- FTC oral solution can be kept at room temperatures up to 77°F (25°C) if used within 3 months; refrigerate for longer term storage.
- Before using FTC, screen patients for HBV.

Metabolism

- Limited metabolism: No cytochrome P (CYP)450 interactions.
- Renal excretion 86%: Competition with other compounds that undergo renal elimination.
- **Dosing of FTC in patients with renal impairment:** Decrease dosage in patients with impaired renal function. Consult manufacturer's prescribing information.
  - Do not use Atripla (fixed-dose combination) in patients with creatinine clearance (CrCl) <50 mL/min or in patients requiring dialysis.
  - Do not use Truvada (fixed-dose combination) in patients with CrCl <30 mL/min or in patients requiring dialysis.

Drug Interactions (See also the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.)***:***

- *Other nucleoside reverse transcriptase inhibitors (NRTIs):* Do not use emtricitabine in combination with lamivudine because the agents share similar resistance profiles and lack additive benefit.
- *Renal elimination:* Competition with other compounds that undergo renal elimination (possible competition for renal tubular secretion). Drugs that decrease renal function could decrease clearance.

Major Toxicities:

- *More common:* Headache, insomnia, diarrhea, nausea, rash, and hyperpigmentation/skin discoloration (possibly more common in children).
- *Less common (more severe):* Neutropenia. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported. Exacerbations of hepatitis have occurred in HIV/HBV-coinfected patients who changed from emtricitabine-containing to non-emtricitabine-containing regimens.

Resistance: The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations (see http://www.iasusa.org/resistance_mutations/index.html) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see http://hivdb.stanford.edu/pages/GRIP/FTC.html).

Pediatric Use: Emtricitabine is Food and Drug Administration (FDA) approved for once-daily administration in children starting at birth. Owing to its once-a-day dosing, minimal toxicity, and pediatric pharmacokinetic (PK) data, emtricitabine is commonly used as part of a dual-NRTI backbone in combination antiretroviral therapy (cART).

A single-dose PK study of emtricitabine liquid solution and capsules was performed in 25 HIV-infected children 2–17 years of age[1]. Emtricitabine was found to be well absorbed following oral administration, with a mean elimination half-life of 11 hours (range 9.7 to 11.6 hours). Plasma concentrations in children receiving the 6 mg/kg emtricitabine once-daily dose were approximately equivalent to concentrations in adults receiving the standard 200-mg dose.

Based on this dose-finding study, emtricitabine was given at a dose of 6 mg/kg once daily in combination with other antiretroviral (ARV) drugs[2-3]. PK results were similar to the preceding dose-finding study[1]. Follow-up data extending to Week 96 indicated that 89% of the ARV-naive and 76% of the ARV-experienced children maintained suppression of plasma HIV RNA <400 copies/mL (74% of ARV-naive children and 62% of ARV-experienced children at <50 copies/mL). Minimal toxicity was observed in this trial.

In PACTG P1021, emtricitabine at a dose of 6 mg/kg (maximum 240 mg/day as liquid or 200 mg/day as capsules) in combination with didanosine and efavirenz, all given once daily, was studied in 37 ARV-naive HIV-infected children 3 months to 21 years of age[2]. Eighty-five percent of children achieved HIV RNA <400 copies/mL and 72% maintained HIV RNA suppression to <50 copies/mL through 96 weeks of therapy. The median CD4 count rose by 329 cells/mm^3 at Week 96.

A study in South Africa evaluated the PKs of emtricitabine in 20 HIV-exposed infants <3 months of age, given emtricitabine as 3 mg/kg once daily for two 4-day courses, separated by an interval of ≥2 weeks[4]. Emtricitabine exposure (area under the curve [AUC]) in neonates receiving 3 mg/kg emtricitabine once daily was in the range of pediatric patients >3 months of age receiving the recommended emtricitabine

dose of 6 mg/kg once daily and adults receiving the once-daily recommended 200 mg emtricitabine dose (AUC approximately 10 hr*ug/mL). Over the first 3 months of life, emtricitabine AUC decreased with increasing age correlating with an increase in total body clearance of the drug. No safety issues were identified in this short PKs study; however, extensive safety data are lacking in this age group.

References

1. Wang LH, Wiznia AA, Rathore MH, et al. Pharmacokinetics and safety of single oral doses of emtricitabine in human immunodeficiency virus-infected children. *Antimicrob Agents Chemother.* 2004;48(1):183-191.
2. McKinney RE, Jr., Rodman J, Hu C, et al. Long-term safety and efficacy of a once-daily regimen of emtricitabine, didanosine, and efavirenz in HIV-infected, therapy-naive children and adolescents: Pediatric AIDS Clinical Trials Group Protocol P1021. *Pediatrics.* 2007;120(2):e416-423.
3. Saez-Llorens X, Violari A, Ndiweni D, et al. Long-term safety and efficacy results of once-daily emtricitabine-based highly active antiretroviral therapy regimens in human immunodeficiency virus-infected pediatric subjects. *Pediatrics.* 2008;121(4):e827-835.
4. Blum M, Ndiweni D, Chittick G, et al. Steady state pharmacokinetic evaluation of emtricitabine in neonates exposed to HIV in utero. Paper presented at: 13th Conference on Retroviruses and Opportunistic Infections (CROI); February 5-9, 2006; Denver, CO. Abstract 568.